## REMARKS

Claims 5 to 18 are pending in the instant application. By this amendment, claims 7 and 9 have been cancelled without prejudice to applicant's right to pursue the subject matter of the cancelled claims in this or other applications. Claims 5, 8, 10 to 13, and 18 have been amended to clarify the invention, and new claims 19 to 21 have been added. In particular, for consistency and clarity, claims 5, 8, and 10 have been amended to replace the phrase "periodontal-infection-induced systemic disease" with the equivalent phrase "oral bacterial-mediated systemic disease;" claims 8 and 11 have been amended to specify additional therapeutic agents; and claims 13 and 18 have been amended to correct informalities and typographical errors. The amended and new claims are fully supported by the specification and claims as originally filed (see, in particular, original claims 5, 6, and 8 and p. 29, *l.* 32 - p. 32, *l.* 8 and p. 15, *ll.* 3-8).

Accordingly, claims 5, 6, 8, and 10 to 21 will be pending upon entry of the instant amendment. Thus, no new matter is added by this amendment. Applicants respectfully request that the amendments and remarks made herein be entered into the record of the instant application.

### 1. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, FOR LACK OF ENABLEMENT, SHOULD BE WITHDRAWN

Claims 8 and 12 are rejected for lack of enablement for "an additional therapeutic agent". In response, Claims 8 and 12 have been amended to recite a Markush group of known therapeutic agents. Support for this amendment is provided in the specification on page 29, line 32 to page 32, line 8. Therefore, Applicants submit that one of skill in the art would know what is included and excluded by the term 'additional therapeutic agent' recited in amended claims 8 and 12.

Claims 5 to 18 are rejected for lack of enablement. As amended, claims 5, 6, 8, and 10-21 recite methods for using compositions effective for controlling bacterial infection in the oral cavity and inhibiting oral bacteria-mediated systemic disease. Applicants submit that the specification teaches in great detail how to make and use each of these known components for controlling bacterial infections (see specification pp. 13 to 35, *l.* 9, and the Examples at p. 35, *l.* 10, to p. 38), and further teaches how to combine these ingredients to

control and treat oral bacteria-mediated systemic disease such that one of skill in the art is able to make and use the claimed invention.

According to the Examiner, the claims include Markush groups of antimicrobial agents, different forms of the composition, and H2 antagonists and/or additional therapeutic agents, but the specification fails to teach how to make and use each and every of the components in each of the claimed forms. The Examiner contends that one of skill in the art would not be able to determine the amounts, proportions or combinations for the antimicrobial agents specified in claim 5.

Applicants submit that each of the antimicrobial agents specified in amended claims 5, 6, 8, and 10-21 are well known to the skilled artisan, and the specification teaches that the effective amount of microbial agent "will vary with particular condition being treated, the age and physical condition of the patient being treated, the severity of the condition, the duration of treatment, the nature of concurrent therapy, the specific from (*i.e.*, salt) of the antimicrobial agent employed, and the particular vehicle from which the antimicrobial agent is applied." (see specification at p. 11, *ll.* 25-29.) The specification provides ranges for effective dosages of antimicrobial agents, which vary depending on the particular antimicrobial agent and the particular composition (see specification, p.13, *l.*19 - p.17, *l.*13 and p.32, *l.*9 - p. 35, *l.*9 and working examples on pp. 35-38). For example, the specified amount of chlorite ion for use in dentifrice and mouthwash compositions can range from greater than about 0.02% by weight (see specification, p.15, *ll.*18-25), preferably from about 0.02% to about 6.0%, and the specified dosage for stannous ions as microbial agent in the range of from about 0.25% to about 11% by weight of final composition (see specification p.13, *l.*32 - p.14, *l.*4).

Following the guidance provided in the instant specification and knowledge in the art, the skilled practitioner can readily determine, the appropriate dosages to be administered to any particular subject or patient, without undue experimentation.

Therefore, in view of the disclosure in the instant specification, and the level of skill in the art, applicants respectfully request the Examiner's withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, for lack of enablement.

## 2. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, FOR LACK OF WRITTEN DESCRIPTION, SHOULD BE WITHDRAWN

Claims 10 to 12 are rejected under 35 U.S.C § 112 first paragraph as failing to comply with the written description requirement, as allegedly containing new matter. In particular, the Examiner contends that the limitation "in the absence of an H2 antagonist" is new matter because the specification as originally filed specifies that H2 antagonists may be included, and therefore a negative limitation such as excluding a component is nto found in the specification..

Applicants respectfully disagree with the Examiner's characterization of claims 10 to 12. Claims 10 to 12 specify that "the *amount of antimicrobial agent* is an amount effective to control bacterial infection in the oral cavity and inhibit oral bacteria-mediated systemic disease in the absence of H2 antagonist." This language does not exclude an H2 antagonist *per se*, but, rather, specifies how the *effective amount* of antimicrobial agent is measured, *i.e.*, in the absence of H2 antagonist. The claimed amount of antimicrobial agent effective to control bacterial infection in the oral cavity and inhibit oral bacteria-mediated systemic disease in the absence of H2 antagonist is supported by the specification, including the examples, as originally filed (see specification p.13, *l.*19 - p.17, *l.*13 and p.32, *l.*9 - p.38). Thus, applicants respectfully request the Examiner's withdrawal of the rejection.

## 3. THE REJECTION UNDER 35 U.S.C. § 102(b) SHOULD BE WITHDRAWN

Claims 5 to 9 are rejected under 35 U.S.C. § 102(b) as anticipated by Singer, which discloses a method or treatment of gingivitis or periodontitis comprising the topical administration to the oral cavity of a composition comprising an H2 antagonist and, optionally, an antimicrobial anti-plaque agent and a pharmaceutically acceptable carrier. The Appeal Board rejected the claims under appeal, holding that the purported new use of promoting whole body health did not constitute a patentable difference because the preamble offered no distinct definition of the claimed invention's limitations. As discussed in detail below, the amended claims obviate this rejection.

Amended Claims 5, 6, and 8 recite methods for administering an antimicrobial agent in an amount effective to *control bacterial infection in the oral cavity and inhibit oral*

*bacteria-mediated systemic disease* in human and other animal subjects *having or at risk of developing an oral bacterial-mediated periodontal systemic disease.*

Singer relates to the use of H2 antagonists, and as such, is not relevant art to the instant invention as claimed in amended claims 5, 6, and 8, which do not include the use of H2 antagonists. Singer does not disclose treatment of the subjects specified in the claims, nor does it disclose amounts effective to inhibit oral bacteria-mediated systemic disease. Instead, Singer discloses a method for preventing and treating *inflammation* in the oral cavity (*i.e.*, inflammation of the gums (gingivitis) and soft tissue aspects of periodontitis) by topical treatment of the oral cavity with a composition comprising an H2 antagonist and *optionally* an antimicrobial anti-plaque agent. Applicants submit that the Singer method does not anticipate the claimed method for several reasons.

Singer does not disclose treating the patient population specified by the claims -- human and other animal subjects *having or at risk of developing an oral bacteria-mediated systemic disease.* Second, Singer describes treating oral inflammation -- not the indication set forth in the claims -- *i.e.*, bacteria-mediated systemic disease. Third, Singer does not describe using an amount of antimicrobial agent effective to *control bacterial infection in the oral cavity and inhibit oral bacteria-mediated systemic disease* because performing the method of Singer (even with the optional combination of an H2 antagonist and an antimicrobial agent) would not necessarily result in treatment of such conditions, as discussed in detail below.

Thus, Applicants assert that the Singer method for treating oral inflammation does not anticipate either explicitly or inherently, amended claims 5, 6, and 8 of treating patients having or at risk of developing an oral bacteria-mediated systemic disease by using an amount of antimicrobial agent effective to control bacterial infection in the oral cavity and inhibit oral bacteria-mediated systemic disease because performing the method of Singer would not necessarily result in treatment of such conditions.

It is submitted that claims 10 to 12, which recite an amount of antimicrobial agent effective to control bacterial infection in the oral cavity and inhibit oral bacteria-mediated systemic disease in the absence of H2 antagonist, and new claims 13 to 18, which recite the additional limitation of a method comprising the step of assessing one or more whole body

health indices or biomarkers in said human and other animal subject, are not disclosed nor suggested by Singer.

Therefore, applicants respectfully request the withdrawal of the rejection under 35 U.S.C. § 102(b).

## 4. THE REJECTION UNDER 35 U.S.C. § 103(a) SHOULD BE WITHDRAWN

Claims 10 to 12 are rejected under 35 U.S.C. § 103(a) as rendered obvious in view of Singer. The Examiner contends that the claims are different from Singer in that they exclude H2 antagonists, and that it would have been obvious to one of ordinary skill in the art at the time of the invention to make oral care products containing other standard components with or without H2 antagonists.

As noted above, Applicants respectfully disagree with the Examiner's characterization of claims 10 to 12. Claims 10 to 12 specify "an *amount of antimicrobial agent* is an amount effective to control bacterial infection in the oral cavity and inhibit oral bacteria-mediated systemic disease in the absence of H2 antagonist." This language does not exclude an H2 antagonist *per se*, but, rather, specifies how the *effective amount* of antimicrobial agent is measured, *i.e.*, in the absence of H2 antagonist.

Applicants submit that the Examiner has not met his burden of establishing a *prima facie* case of obviousness of the claimed methods reciting the use of compositions having an *amount of antimicrobial agent* specified by the claims, *i.e.*, an amount effective to control bacterial infection in the oral cavity and inhibit oral bacteria-mediated systemic disease in the absence of H2 antagonist. As such, applicants believe the rejection is in error and request its withdrawal.

Claims 13 to 18 are also rejected under 35 U.S.C. § 103(a) as unpatentable in view of Singer. The Examiner contends that the claims are different from Singer in that they specify particular markers of body health. The Examiner further contends that it would be obvious to one of ordinary skill in the art at the time of the invention "to employ any known marker of body health as an indicator of body health because all the claimed markers are empolyed in this art in some fashion as markers of some dysfunction or disorder."

However, the Examiner has not presented any evidence that one of ordinary skill in the art at the time the invention was made would have had any motivation to inhibit systemic

disease mediated by oral bacteria. This is due to the simple fact that, prior to the instant invention, no one appreciated that bacterial infections of the oral cavity were the cause of such systemic disease. The inventors discovered that periodontal infection stimulates a systemic response, including inflammatory and acute immune responses, caused by the spread of oral pathogenic bacteria, associated bacterial toxins and endotoxins and inflammatory cytokines and mediators prompted by these oral pathogens. This oral bacteria infection-stimulated systemic response can result in various diseases and conditions such as cardiovascular disease, stroke, atherosclerosis, diabetes, severe respiratory infections, premature births and low birth weight, post-partum dysfunction in neurologic and developmental functions, and associated increased risk of mortality. These systemic diseases and conditions can be protected against by treating and preventing diseases and conditions of the oral cavity using the methods described and claimed in the instant application.

Thus, prior to the instant invention, there was no motivation for the use indicators of whole body health in connection with the claimed methods for using oral treatments. Therefore, applicants respectfully request the withdrawal of the rejection under 35 U.S.C. § 103(a).

## 5. THE REJECTION UNDER 35 U.S.C. § 101 SHOULD BE WITHDRAWN

The claims are rejected under 35 U.S.C. § 101 as inoperative and lacking utility. The Examiner contends that no evidence or examples are given for promoting whole body health in any human or any animal using the claimed methods, so the intended use is not specific, credible, and substantial.

The Examiner states that the present claims are directed to treating humans specifically to promote whole body heath by administering known antimicrobial agents. The Examiner further states that the results are directed to treating periodontal infection which is not claimed. Applicants respectfully disagree, as discussed below.

The pending claims relate to methods comprising an amount of an antimicrobial agent effective to control bacterial infection in the oral cavity and inhibit oral bacteria-mediated systemic disease. Thus, the claimed methods are not "directed to treating periodontal infection which is not claimed" as contended by the Examiner. Rather, the claims are

specifically directed to controlling bacterial infection in the oral cavity as a means of treating a systemic disease, which is precisely the result demonstrated by the Offenbacher Declaration filed January 19, 2005.

As such, for the reasons presented above, Applicants respectfully request that the rejection under 35 U.S.C. § 101 be withdrawn.

## 6. THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, FOR INDEFINITENESS, SHOULD BE WITHDRAWN

Claims 7, 9, 13, and 18 are rejected under 35 U.S.C. § 112, second paragraph, for being indefinite. In response, claims 7, 9, 13, and 18 have been amended to correct typographical errors and particularly point out and distinctly claim the invention.

Thus, Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph, be withdrawn.

## 7. NEW CLAIMS 19, 20, AND 21

New claims 19-21 have been added to recite a method that excludes the use of an H2 antagonist as an additional therapeutic agent. This claim limitation is fully supported by the specification and claims as originally filed (see, in particular, original Claims 5, 6, and 8 and p. 29, *l.* 32 - p. 32, *l.* 8 and p. 15, *ll.* 3-8), which discloses and provides extensive examples the genus of additional therapeutic agents. According to the M.P.E.P., a negative limitation is properly supported by a positive recitation of alternative elements. See Section 2173.05(i) of The Manual of Examination Procedure ("M.P.E.P."), 8th Edition, Revision 3, August 2005, which states that "If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims." See *In re Johnson*, 558 F.2d 1008, 1019, 194 U.S.P.Q. 187 (C.C.P.A. 1977), ("[the] specification, having described the whole, necessarily described the part remaining."). See also *Ex parte Grasselli*, 231 USPQ 393 (Bd. App. 1983), aff'd mem., 738 F.2d 453 (Fed. Cir. 1984). The *Johnson* court upheld support for the proviso language in a claim, based on the specification having "a broad and complete generic disclosure, coupled with extensive examples." *Johnson* at 196. The *Johnson* court held that the "specification supported the claims *in the absence of the limitation*, and that specification, having described the whole, necessarily described the part remaining." [*Emphasis added*] *Id.* at 197.

As such, new claims 19, 20, and 21 are fully supported by the written description of the specification as originally filed.

## CONCLUSION

In light of the amendments and remarks above, applicants estimate that the pending claims are allowable. Applicants respectfully request that the foregoing amendments and remarks in be made of record in the instant application.

Respectfully submitted,

Date: June 22, 2006

Laura A. Coruzzi 30,742
Laura A. Coruzzi (Reg. No.)

By: Eileen E. Falvey 46,097
Eileen E. Falvey (Reg. No.)

**JONES DAY**
222 East 41st Street
New York, New York 10017
(212) 326-3939